

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) Haitao Wu et al.

Attorney Docket No.: BSA 04-02

For: CARBORANYLPORPHYRINS AND USES THEREOF

Mail Stop Patent Application
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

In order to fulfill the requirements of candor and good faith set forth in 37 C.F.R.

§1.56, Applicants submit herewith the following Information Disclosure Statement in
accordance with the provisions of 37 C.F.R. §1.97 and §1.98.

UNITED STATES PATENT PUBLICATIONS

<u>PATENTEE</u>	<u>PUBLICATION NO.</u>	<u>PUBLICATION DATE</u>
Miura et al.	2003/0032799 A1	Feb. 13, 2003
Miura et al.	2003/0083494 A1	May 1, 2003

UNITED STATES PATENTS

<u>PATENTEE</u>	<u>PATENT NO.</u>	<u>ISSUE DATE</u>
Lavallee et al.	4,783,529	Nov. 8, 1988
Miura et al.	4,959,356	Sep. 25, 1990
Kahl et al.	5,149,801	Sep. 22, 1992
Cole et al.	5,162,231	Nov. 10, 1992
Mauclaire et al.	5,268,371	Dec. 7, 1993
Bhardwaj et al.	5,312,896	May 17, 1994

Bodaness	5,563,132	Oct. 8, 1996
Kahl et al.	5,654,423	Aug. 5, 1997
Maier et al.	5,674,467	Oct. 7, 1997
Miura et al.	5,877,165	Mar. 2, 1999
Sessler et al.	5,955,586	Sep. 21, 1999
Scanlon, Jr. et al.	6,010,805	Jan. 4, 2000
Stojiljkovic et al.	6,066,628	May 23, 2000
Miura et al.	6,566,517 B2	May 20, 2003

FOREIGN PATENT DOCUMENTS

<u>COUNTRY</u>	<u>PUBLICATION NO.</u>	<u>PUBLICATION DATE</u>
PCT	WO 01/85736 A1	Nov. 15, 2001

NON-PATENT PUBLICATIONS

1. Morris et al., "Porphyrin-mediated boron neutron capture therapy: evaluation of the reactions of skin and central nervous system," *Int. J. Radiat. Biol.*, 79(3): 149-158 (2003).
2. Vincente, et al., "Synthesis, dark toxicity and induction of *in vitro* DNA photodamage by a tetra (4-*nido*-carboranylphenyl)prophyrin," *J. Photochem. Photobiol. B. Biology*, 68(2-3): 123-132 (2002).
3. Maderna et al., "Synthesis of a porphyrin-labelled carboranyl phosphate diester: a potential new drug for boron neutron capture therapy of cancer," *Chem. Commun.*, 16: 1784-1785 (2002).
4. Miura et al., "Boron Neutron Capture of a Murine Mammary Carcinoma using a Lipophilic Carboranyltetraphenylporphyrin," *Radiat. Res.*, 155(4): 603-610 (2001).
5. Miura et al., "Evaluation of carborane-containing porphyrins as tumor targeting agents for boron neutron capture therapy," *Br. J. Radiol.*, 71(847): 773-781 (1998).

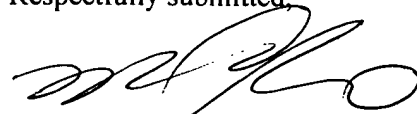
6. Miura et al., "Synthesis of a Nickel Tetracarboranylphenylporphyrin for Boron Neutron-Capture Therapy: Biodistribution and Toxicity in Tumor-Bearing Mice," *Int. J. Cancer*, 68(1): 114-119 (1996).
7. Kahl et al., "A Carboranyl Porphyrin for Boron Neutron Capture Therapy of Brain Tumors," *Basic Life Sci.*, 50: 193-203 (1989).
8. Miura et al., "Biodistribution of copper carboranyltetraphenylporphyrins in rodents bearing an isogeneic or human neoplasm," *J. NeuroOncol*, 5: 111-117 (2001).
9. Berlin et al., "Are Porphyrin Mixtures Favorable Photodynamic Anticancer Drugs? A Model Study with Combinatorial Libraries of Tetraphenylporphyrins," *Combinatorial Chemistry*, 61(2): 107-118 (1998).
10. Miller et al., "In Vivo Animal Studies with Gadolinium (III) Texaphyrin As a Radiation Enhancer," *Int. J. Radiat. Oncol. Biol. Phys.*, 45(4): 981-989 (1999).
11. Bhyrappa et al., "Octabromotetraphenylporphyrin and Its Metal Derivatives: Electronic Structure and Electrochemical Properties," *Inorg. Chem.*, 30: 239-245 (1991).
12. Birnbaum et al., "¹⁹F NMR Spectra and Structures of Halogenated Porphyrins," *Inorg. Chem.*, 34(14): 3625-3632 (1995).
13. Fairchild et al., "Current Status of ¹⁰B-Neutron Capture Therapy: Enhancement of Tumor Dose Via Beam Filtration and Dose Rate, and the Effects of These Parameters on Minimum Boron Content: a Theoretical Evaluation," *Int. J. Radiat. Oncol. Biol. Phys.*, 11(4): 831-840 (1985).
14. Woller et al., "2, 3, 7, 8, 12, 13, 17, 18-Octafluoro-5, 10, 15, 20-tetraarylporphyrins and Their Zinc Complexes: First Spectroscopic, Electrochemical, and Structural Characterization of a Perfluorinated Tetraarylmetalloporphyrin," *J. Org. Chem.*, 62(6): 1588-1593 (1997).
15. Woller et al., "A Straightforward Synthesis of 3,4-Difluoropyrrole," *J. Org. Chem.*, 63(16): 5706-5707 (1998).
16. Ozette et al., "New Metalloporphyrins with Extremely Altered Redox Properties: Synthesis, Structure, and Facile Reduction to Air-Stable π -Anion Radicals of Zinc and Nickel β -Heptanitroporphyrins," *J. Am. Chem. Soc.*, 119(27): 6442-6443 (1997).
17. Chanana et al., "Boron Neutron Capture Therapy for Glioblastoma Multiforme: Interim Results from the Phase I/II Dose-Escalation Studies," *Neurosurgery*, 44(6): 1182-1193 (1999).

18. Vincente et al., "Syntheses of carbon – carbon linked carboranylated porphyrins for boron neutron capture therapy of cancer." *Tetrahedron Letters*, 41: 7623-7627 (2000).
19. Evstigneeva, "Synthesis of Carboranylporphyrins and the Perspectives of Their Use for Boron Neutron Capture Therapy," *Molecules*, 5: 1479-80 (2001).
20. Zakharkin et al., "Synthesis of carboranyl derivatives of deuteroporphyrin IX," *Russian Chemical Bulletin*, 48(12): 2312-14 (1999).
21. "Brain Tumor Patients Offered New Hope with Expanded Trial of Promising Therapy," Press Release, Brookhaven National Labs, Nov. 1998, <<http://virtualtrials.com/bnct2.cfm>>.
22. Yarris, "Accelerator for Boron Neutron Capture Therapy Proposed by Lab," Jun. 21, 1996, Lawrence Berkeley National Laboratory, <<http://www.lbl.gov/Science-Articles/Archive/boron-capture.html>>.
23. Gomez, "Boron Neutron Capture Therapy (BNCT)," Dec. 1, 1998, Lawrence Berkeley National Laboratory, <<http://www.virtualtrials.com/bnct.cfm>>.
24. Chu et al., Overview - LBNL/UCSF Boron Neutron Capture Proposal, <<http://ehs.lbl.gov/bnct/overview.html>>.
25. Chu et al., Work in Progress – LBNL/UCSF Boron Neutron Capture Proposal, "Progress Report (4/97) on 'Accelerator-Based BNCT Clinical Trial'," <<http://ehs.lbl.gov/bnct/progress.html>>.
26. Ludewigt et al., "Research Topics and Papers, Neutron Production Target for the BNCT Project at Lawrence Berkeley National Laboratory and at the University of California at San Francisco, Project 2b – Neutron Production Target," <<http://ehs.lbl.gov/bnct/research/target.html>>.
27. Larson et al., "Research Topics and Papers, Phase I Study Concept for the BNCT Project at Lawrence Berkeley National Laboratory and at the University of California at San Francisco, Project 11 – Proposed BNCT Clinical Trials," <<http://ehs.lbl.gov/bnct/research/proposedtrials.html>>.
28. Deen et al, "Research Topics and Papers, Small Animal and *In Vitro* Toxicity and Biodistribution for the BNCT Project at Lawrence Berkeley National Laboratory and at the University of California at San Francisco, Project 6- Small Animal and *In Vitro* Toxicity, Biodistribution and Radiobiology," <http://ehs.lbl.gov/bnct/research/smallanimal.html>>.
29. Fike et al, "Research Topics and Papers, Small Animal and *In Vitro* Toxicity and Biodistribution for the BNCT Project at Lawrence Berkeley National Laboratory and at the University of California at San Francisco, Project 7- Large Animal Pharmacology and Toxicology," <http://ehs.lbl.gov/bnct/research/largeanimal.html>>.

The above-referenced documents are listed on PTO Form 1449. We have enclosed the cited documents to facilitate reference to them.

Applicants are not aware of any other references to be identified at this time. If the Examiner has any questions or comments relating to the present application, he or she is respectfully invited to contact Applicants' attorney at the telephone number set forth below.

Respectfully submitted,



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FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (Rev. 2-32) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)	ATTY. DOCKET NO. BSA 04-02	SERIAL NO. Unassigned
	APPLICANT Haitao Wu et al.	CONFIRMATION NO. Unassigned
	FILING DATE Concurrently	GROUP Unassigned

U.S. PATENT PUBLICATIONS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPROPRIATE
		2003/0032799 A1	2-13-03	Miura et al.			
		2003/0083494 A1	5-1-03	Miura et al.			

U.S. PATENT DOCUMENTS

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		4,783,529	11-8-88	Lavallee et al.			
		4,959,356	9-25-90	Miura et al.			
		5,149,801	9-22-92	Kahl et al.			
		5,162,231	11-10-92	Cole et al.			
		5,268,371	12-7-93	Mauclair et al.			
		5,312,896	5-17-94	Bhardwaj et al.			
		5,563,132	10-8-96	Bodaness			
		5,654,423	8-5-97	Kahl et al.			
		5,674,467	10-7-97	Maier et al.			
		5,877,165	3-2-99	Miura et al.			
		5,955,586	9-21-99	Sessler et al.			
		6,010,805	1-4-00	Scanlon, Jr. et al.			
		6,066,628	5-23-00	Stojiljkovic et al.			
		6,566,517	5-20-03	Miura et al.			

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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION	
							YES	NO
		WO 01/85736 A1	11-15-01	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

1.		Morris et al., "Porphyrin-mediated boron neutron capture therapy: evaluation of the reactions of skin and central nervous system," <i>Int. J. Radiat. Biol.</i> , 79(3): 149-158 (2003).
2.		Vincente, et al., "Synthesis, dark toxicity and induction of <i>in vitro</i> DNA photodamage by a tetra (4- <i>nido</i> -carboranylphenyl)prophyrin," <i>J. Photochem. Photobiol. B. Biology</i> , 68(2-3): 123-132 (2002).
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5.		Miura et al., "Evaluation of carborane-containing porphyrins as tumor targeting agents for boron neutron capture therapy," <i>Br. J. Radiol.</i> , 71(847): 773-781 (1998).
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9.	Berlin et al., "Are Porphyrin Mixtures Favorable Photodynamic Anticancer Drugs? A Model Study with Combinatorial Libraries of Tetraphenylporphyrins," <i>Combinatorial Chemistry</i> , 61(2): 107-118 (1998).
10.	Miller et al., "In Vivo Animal Studies with Gadolinium (III) Texaphyrin As a Radiation Enhancer," <i>Int. J. Radiat. Oncol. Biol. Phys.</i> , 45(4): 981-989 (1999).
11.	Bhyrappa et al., "Octabromotetraphenylporphyrin and Its Metal Derivatives: Electronic Structure and Electrochemical Properties," <i>Inorg. Chem.</i> , 30: 239-245 (1991).
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18.	Vincente et al., "Syntheses of carbon - carbon linked carboranylated porphyrins for boron neutron capture therapy of cancer." <i>Tetrahedron Letters</i> , 41: 7623-7627 (2000).
19.	Evstigneeva, "Synthesis of Carboranylporphyrins and the Perspectives of Their Use for Boron Neutron Capture Therapy," <i>Molecules</i> , 5: 1479-80 (2001).
20.	Zakharkin et al., "Synthesis of carboranyl derivatives of deuteroporphyrin IX," <i>Russian Chemical Bulletin</i> , 48(12): 2312-14 (1999).
21.	"Brain Tumor Patients Offered New Hope with Expanded Trial of Promising Therapy," Press Release, Brookhaven National Labs, Nov. 1998, < http://virtualtrials.com/bnct2.cfm >.
22.	Yarris, "Accelerator for Boron Neutron Capture Therapy Proposed by Lab," Jun. 21, 1996, Lawrence Berkeley National Laboratory, < http://www.lbl.gov/Science-Articles/Archive/boron-capture.html >.

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24.	Chu et al., Overview - LBNL/UCSF Boron Neutron Capture Proposal, < http://ehs.lbl.gov/bnct/overview.html >.
25.	Chu et al., Work in Progress - LBNL/UCSF Boron Neutron Capture Proposal, "Progress Report (4/97) on 'Accelerator-Based BNCT Clinical Trial'," < http://ehs.lbl.gov/bnct/progress.html >.
26.	Ludewigt et al., "Research Topics and Papers, Neutron Production Target for the BNCT Project at Lawrence Berkeley National Laboratory and at the University of California at San Francisco, Project 2b - Neutron Production Target," < http://ehs.lbl.gov/bnct/research/target.html >.
27.	Larson et al., "Research Topics and Papers, Phase I Study Concept for the BNCT Project at Lawrence Berkeley National Laboratory and at the University of California at San Francisco, Project 11 - Proposed BNCT Clinical Trials," < http://ehs.lbl.gov/bnct/research/proposedtrials.html >.
28.	Deen et al, "Research Topics and Papers, Small Animal and <i>In Vitro</i> Toxicity and Biodistribution for the BNCT Project at Lawrence Berkeley National Laboratory and at the University of California at San Francisco, Project 6- Small Animal and <i>In Vitro</i> Toxicity, Biodistribution and Radiobiology," http://ehs.lbl.gov/bnct/research/smallanimal.html >.
29.	Fike et al, "Research Topics and Papers, Small Animal and <i>In Vitro</i> Toxicity and Biodistribution for the BNCT Project at Lawrence Berkeley National Laboratory and at the University of California at San Francisco, Project 7- Large Animal Pharmacology and Toxicology," http://ehs.lbl.gov/bnct/research/largeanimal.html >.

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